Supplementary methods

Neuropsychological assessment

Participants were cognitively assessed at baseline and at follow-up using a large battery of neuropsychological tests, including global cognition, memory, attention, language, executive function and visuospatial function. The performance of each group was compared with that of a reference group of age-matched healthy controls (Bergman *et al.*, 2007), and expressed as z-scores. The delay between the PET scan and the neuropsychology assessment was 3.4 ± 2.7 months.

Global cognition was estimated using the mini-mental state examination (MMSE) score at baseline, along with a composite measure calculated as the average performance score from nine tests, including five subtests from the Weschler Adult Intelligence Scale: Similarities (abstract verbal reasoning), Information (semantic memory), Block Design (visuospatial function), Digit Span (verbal short-term memory, forward and backward), Digit Symbol (visuospatial short-term memory); as well as the Corsi test (visuospatial short-term memory), the Trailmaking A and B tests (attention/executive function) and the copy of the Rey-Osterrieth complex figure test (RCFT: visuospatial function). Episodic memory performance was computed as the average performance score from the following three tests: Rey-Auditory Verbal Learning (RAVL) learning and delayed retention, and the RCTF retention subtest (Strauss, 2006). Data on the complete neuropsychological examination will be reported elsewhere.

CSF analysis

CSF samples were analyzed as previously described (Carter *et al.* , 2012). All sporadic and sMC patients underwent CSF sampling. CSF data for pMC and NC subjects has been published previously (Thordardottir *et al.* , 2014).

PET and MRI image acquisition

All 52 participants underwent PET scans at baseline with the three tracers, except for three participants, who for technical or personal reasons missed one of the PET scans with ^{11}C-PiB, ^{11}C-DED, and ^{18}F-FDG, respectively. At follow-up, all 26 participants underwent PET scans with the three tracers, except for one individual who missed the ^{18}F-FDG and ^{11}C-DED scans, another individual who missed a ^{11}C-PiB scan, and a third subject who missed a ^{11}C-DED scan.

The mean injected doses for each tracer were 221 ± 65 MBq for ^{11}C-DED, 227 ± 76 MBq for ^{11}C-PiB, and 229 ± 42 MBq for ^{18}F-FDG. Participants fasted for 4 hours preceding the ^{18}F-FDG scan. All but two PET scans were obtained within a period of 20 days for each participant. ^{11}C-DED and ^{11}C-PIB PET acquisitions lasted 60 minutes each, and ^{18}F-FDG acquisition lasted 45 minutes. The frames were realigned for all the tracers and used to create late-sum images: from 10 to 60 minutes post-injection for ^{11}C-DED, 40 to 60 minutes for ^{11}C-PIB, and 30 to 45 minutes for ^{18}F-FDG.

All participants also underwent a structural T1 MRI sequence (Siemens Trio scanner 3T) at baseline. Because the 14 healthy controls were recruited from another study, their MRI scans were acquired at 1.5 T on a Philips Intera scanner (see Carter et al. (Carter *et al.*, 2012) for more information on healthy control recruitment and MRI image acquisition parameters).

References

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